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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,197	12/09/2005	Richard Joseph Fagan	C & R-104	1804

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
11/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,197	FAGAN ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-69* is/are pending in the application.

4a) Of the above claim(s) *49-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48 and 67-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20061002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

described by the claims known to the inventors at the time the application was filed. It is agreed that the polypeptide having the amino acid sequence set forth in SEQ ID NO:22 comprises two catalytic domains each of which shares a significant degree of amino acid sequence homology with members of the trypsin family of serine proteases, yet claims 48 and 67-69 lack utility because there is no disclosure in the specification of any specific and substantial *in vitro* utility for an isolated polypeptide having the amino acid sequence set forth in SEQ ID NO:22, and the specification discloses no specific and substantial *in vivo* utility for an isolated polypeptide having the amino acid sequence set forth in SEQ ID NO:22.

Specifically, the specification cannot identify any particular substrate that is recognized and cleaved by either of the proposed serine protease domains within SEQ ID NO:2, whether *in vivo* or *in vitro*, nor can it identify a specific cellular, extracellular, or physiological function provided by either of the proposed serine protease domains. While the specification proposes at page 8, lines 8-12, that "screening methods" may be designed to identify compounds that are effective in the treatment and diagnosis of disease" once some function of the polypeptide having the amino acid sequence of SEQ ID NO:22 has been identified, and further propose a litany of diseases in the paragraph spanning pages 8 and 9 with which the polypeptide having the amino acid sequence of SEQ ID NO:22 might eventually be found to be associated, such suggestions of diagnostic and prognostic uses for the claimed polypeptide are not specific because there is no disclosure of any specific disease state or medical condition that actually can be diagnosed. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific in vivo utility that is substantial. Indeed, the specification's diffuse assertions indicate the contrary, that Applicant knew no specific utility for either native polypeptide encoded by claimed nucleic acid sequences at the time the application was filed that would permit an immediate use by the public of a disclosed nucleic acid sequence, or any use by the public of an expression vector or cell comprising a disclosed nucleic acid sequence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48 and 67-69 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 48 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of the peptides and polypeptides having the particular amino acid sequences set forth in SEQ IDs NOs:2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, and 26, does not reasonably provide enablement for the preparation of generic proteases having amino acid sequences that diverge at as many as 114, or even 57, unspecified positions from the amino acid sequence set forth in SEQ ID NO:22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

At least clauses 7-10 of claim 48 contemplate arbitrary assignments of any or all of amino acid substitutions, additions or deletions in a claimed, generic, protease at as many as 20%, or 10% of the 567 amino acid positions throughout SEQ ID NO:22. This rejection is stated under the first paragraph of the statute because the specification cannot support introduction of such numerous alterations in the amino acid sequence of SEQ ID NO:22, where amino acid insertions, deletions, or substitutions may occur anywhere, in any combination or in any pattern, within SEQ ID NO:22. Mere sequence perturbation cannot enable the design and preparation of a myriad of divergent polypeptides that might be proteases where the specification fails to teach even the nature of the proteolytic activity that is to be retained, e.g., by identifying a substrate. Neither the specification nor the prior art made of record herewith provide adequate guidance for selecting 114, or even 57, amino acid sequence within SEQ ID NO:22 that might be altered, nor the nature of the alterations, that would permit proper folding of either or both of the catalytic domains indicated by the specification that would allow them to retain their undisclosed function(s).

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a **reasonable correlation** must exist **between the scope asserted** in the claimed subject matter and **the scope of guidance the specification provides**. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with

the degree of unpredictability of factors involved in physiological activity of small peptide hormone). **The Federal Circuit has approved this standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).** Applying several of the factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequence of SEQ ID NO:22 to the extent indicated in clauses 7-10 of claim 48,

b) the specification lacks working examples wherein the amino acid sequence of SEQ ID NO:22 is altered to the extent indicated in clauses 7-10 of claim 48,

c) in view of the prior art publications of record herein concerning very similar polypeptides, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class of serine proteases the specification suggests is represented by SEQ ID NO:22 have had as many as 114, or 57, amino acids specifically identified for concurrent modification, as indicated in clauses 7-10 of claim 48.

Thus the scope of subject matter embraced by the phrases, "at least 80%/90% identity with", is unsupported by the present specification even if taken in combination with teachings available in the prior art.

Claims 48 and 67-69 are additionally rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

While the specification discloses particular functional fragments of the polypeptide having the amino acid sequence se forth in SEQ ID NO:22, e.g., SEQ ID NO:26, the specification fails to exemplify or describe the discovery or preparation of the genus of fragmentary or "functionally equivalent" polypeptides that diverge from the polypeptide having the amino acid sequence set forth in SEQ ID NO:22 at as many as 20%, or even 10%, of the 567 amino acid positions therein at any conceivable set of 114, or 57, amino acid positions dispersed in any pattern throughout SEQ ID NO:22, according to clauses 7-10 of claim 48. Indeed, the specification discloses no particular function that must be retained by such randomly altered fragments or equivalents. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The "test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the Inventor had possession at that time of the . . . claimed subject matter", *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983), and, in 2001, the USPTO issued Guidelines governing its analysis of compliance with the written description requirement. In these

Guidelines, the USPTO states that an applicant may comply with the written description requirement by "show[ing] that an Invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . , i.e., complete or partial structure, other physical and/or chemical properties, function characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." **Guidelines**, 66 Fed. Reg. 1099 at 1106 (5 January 2001). The Federal Circuit adopted the USPTO's standard for determining compliance with the written description requirement In *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). The specification does not disclose the design of the broad genus of polypeptides embraced by, at least, clauses 7-10 of claim 48, which state no particular functional or structural requirements, nor does the specification otherwise disclose the source of generic polypeptides meeting the limitations of these clauses.

The following is a quotation of the second paragraph of 35 U.S.C. § 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48 and 67-69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations of "functional equivalent" in claim 48 render the claim, and claims 67-69 depending therefrom, indefinite because they provide no structural basis for a determination of the extent of structural equivalency of a polypeptide to the polypeptide of SEQ ID NO:22 and the term "functional equivalency" is meaningless where the specification discloses no particular function for the polypeptide of SEQ ID NO:22. Thus the artisan and the public seeking to ascertain the metes and bounds of intended subject matter have no starting point with which to determine the structure or the nature of the polypeptide intended by the claims. Deletion of all references to "functional equivalency" will overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 48 and 67 are rejected under 35 U.S.C. § 102(e) as being anticipated by Goddard et al., US 6,916,648, made of record herewith.

Goddard et al. is the US equivalent publication to WO 00/53756, cited in Applicant's IDS filed 2 October 2006, and is available as prior art in view of, at least, the 24 October 2001 filing date of the US utility application on which the patent issued. Goddard et al. disclose, in their SEQ ID NO:132, the amino acid sequence of a human serine protease that shares 89.3% identity with SEQ ID NO:22 from position 39 through position 548, and comprising amino acid sequences identical to those of SEQ IDs NOs:8, 10, 12, 14, 16, and 18 herein, meeting limitations of claims 48 and 67.

Claims 48 and 67 are rejected under 35 U.S.C. § 102(e) as being anticipated by Plowman et al., US 2002/0064856, made of record herewith.

Plowman et al. is the US equivalent publication to WO 02/00860, cited in Applicant's IDS filed 2 October 2006, and is available as prior art in view of the 26 June 2000 filing date of their priority US provisional application. Plowman et al. disclose, in their SEQ ID NO:86, the amino acid sequence of a human serine protease that shares 93.2% identity with SEQ ID NO:22 from position 17 through position 548, and comprising amino acid sequences identical to those of SEQ IDs NOs:4, 6, 8, 10, 12, 14, 16, 18, and 24 herein, meeting limitations of claims 48 and 67.

Claims 48, 67, and 68 are rejected under 35 U.S.C. § 102(e) as being anticipated by Madison et al., US 2003/0134298, made of record herewith.

Available as prior art in view of the 5 July 2001 filing date of their priority US provisional application, Madison et al. disclose, in their SEQ ID NO: 16, the amino acid sequence of a human transmembrane serine protease having significant sequence identity with human matriptase, which amino acid sequence shares 96.7% identity with SEQ ID NO:22 from position 17 through position 567 and comprising amino acid sequences entirely identical both to SEQ ID NO:26 herein as well as SEQ IDs NOs:4, 6, 8, 10, 12, 14, 16, 18, 20 and 24 herein, meeting the limitations of claims 48, 67, and 68. It is noted that amending claims 48, 67, and 68 to require that a polypeptide comprise, or consist of, the amino acid sequence of SEQ ID NO:22 will overcome this and other prior art rejections, as well as rejections of claims herein under 35 U.S.C. § 112, first paragraph, for lack of adequate written description and for lack of enablement as to making, leaving only the issues of a lack of patentable utility under 35 U.S.C. § 101 and lack of enablement as to use under 35 U.S.C. § 112, first paragraph, to be resolved.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner, Art Unit 1656

William W. Moore
2 November 2007

-continued

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cgtggaatga acaatggaag tcaacaaaaa gcagagctta tcgatgataa gcggtcaaac 1260

atgagaattc gcggccgcat aatacgactc actataggga tcatatttat ggtgttatta 1320

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<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(2132)
<223> OTHER INFORMATION: N refers to any nucleotide.

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tcmmmwwttt gaaaaccmyw attatakktr taagsgggcc aaataatcaa tgttggatat 420

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kttwttcatt ggcccgcctg gaatgtgaaa ggaatgggat tgaatggact ggaatgagaa 4260

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<210> SEQ ID NO 32
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<212> TYPE: DNA
<213> ORGANISM: Endobugula sertula
<220> FEATURE:
<221> NAME/KEY: misc_feature
<222> LOCATION: (1)...(4744)
<223> OTHER INFORMATION: N refers to any nucleotide.

<400> SEQUENCE: 32

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tttgactatc ngaatattaa tactttatcg aatatgatcg agaatgaact cgaagctgtt 180

gaggtatagt tatgttagaa gttattaata gatactgcca tggatacgta ttcgtgccag 240

tggtattggc cntagaagaa aaagggtttt ttgacctttt tacaaggaat agatacctta 300

catttgaaaa aataaaaaca gaattaaatg ctaatagtgg ccatcttcaa gtagccttac 360

gcatgttgca gtctgtttca tggatatcat gtgatgataa agggtatgta ctaacagatg 420

cagcggacga aagaaataaa atatctagtg attttataga gctttttaat ttctctatga 480

DETAILED ACTION

Priority

Applicant's claim in the Declaration of Inventorship and in the first page of the specification filed 9 June 2005 to priority under 35 U.S.C. § 119 of the 11 December 2002 filing date of the British patent application No. 0228957.7, and its successor International patent application PCT/GB03/005404 filed 11 December 2003, of which the current application is a National Stage filing under 35 U.S.C. § 371 is hereby acknowledged.

Information Disclosure Statement

Applicant's Information Disclosure Statement [IDS] filed 2 October 2006 is hereby acknowledged.

Preliminary Amendment

Applicant's Preliminary Amendment filed with the application on 9 June 2005 has been entered, canceling claims 1-47 and providing the new claims 48-69.

Election/Restrictions

Applicant's election without traverse of the invention of Group I, comprising claims 48 and 67-69 to the extent that they describe a protease having an amino acid sequence set forth in SEQ ID NO:22 and to compositions comprising same, in the reply filed 25 October 2007 is acknowledged. Claims 49-66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected elected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 25 October 2007.

Claim Objections

Claim 48 is objected to because of the following informalities: Several occurrences of the term "SEQ ID NO" are misstated in claim 48, e.g., at lines 5, 13, 21, 26, 46, 51-52. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48 and 67-69 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility.

A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility, but the instant application cannot identify any specific, substantial, utility for the invention